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INFORMATION DISCLOSURE STATEMENT

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Dated: March 30, 2004 By: Christopher J. Collins

Sir:

The citations listed below, copies will follow under separate cover, may be material to the examination of the above-identified application, and are therefore submitted in compliance with the duty of disclosure defined in 37 C.F.R. §§ 1.56 and 1.97. The Examiner is requested to make these citations of official record in this application.

The following printed publications are referred to in the body of the specification:

- U. S. Patent No. 5,190,632 to Fujimiya *et al.*;
- U. S. Patent No. 5,069,769 to Fujimiya *et al.*;
- U. S. Patent No. 5,137,609 to Manian *et al.*;
- U. S. Patent No. 4,683,195 to Mullis *et al.*;
- U. S. Patent No. 4,241,050 to Barth;
- U. S. Patent No. 4,728,591 to Clark *et al.*;
- U. S. Patent No. 4,802,951 to Clark *et al.*;
- PCT WO90/05785 to Shultz;
- Noren, *et al.*, "A General Method for Site-Specific Incorporation of Unnatural Amino Acids into Proteins," *Science* 244:182-188 (1989);

- Bain, *et al.*, "Site-Specific Incorporation of Nonnatural Residues during In Vitro Protein Biosynthesis with Semisynthetic Aminoacyl-tRNAs," *Biochemistry* 30:5411-21 (1991);
- Promega Technical Bulletin No. 182; tRNA$^{nacend™}$: Non-Radioactive Translation Detection System. 1-16, Sept. 1993;
- Krieg, *et al.*, Photocrosslinking of the signal sequence of nascent preprolactin to the 54-kilodalton polypeptide of the signal recognition particle," *Proc. Natl. Acad. Sci. USA* 83:8604-08 (1986);
- Molecular Cell Biology, J. Darnell *et al.*, Editors. Scientific American Books. N.Y., N.Y. 1991;
- *Current Protocols in Molecular Biology* (F.M. Ausubel et al. editors, Wiley Interscience, 1993), pp. 10-16, 10-77;
- Seong and RajBhandary, "Escherichia coli formylmethione tRNA: Mutations in ^{GGG} sequence conserved in anticodon stem of initiator tRNAs affect initiation of protein synthesis and conformation of anticodon loop," *Proc. Natl. Acad. Sci. USA* 84:334-338 (1987);
- Bruce and Uhlenbeck, "Specific Interaction of Anticodon Loop Residues with Yeast Phenylalanyl-tRNA Synthetase," *Biochemistry* 21:3921-3926 (1982);
- Pratt, "Coupled Transcription-Translation in Prokaryotic Cell-Free System," (*Transcription and Translation*, B.D. Hames and S.J. Higgins, Editors, p. 179-209, IRL Press, Oxford, 1984);
- Spirin, *et al.*, "A Continuous Cell-Free Translation System Capable of Producing Polypeptides in High Yield," *Sci.* 242:1162-64 (1988);
- Felgner *et al.*, "Lipofection: A highly efficient, lipid-mediated DNA-transfection procedure," *Proc. Natl. Acad. Sci. USA* 84:7413-17 (1987);
- Neu and Heppel, "Nucleotide Sequence Analysis of Polyribonucleotides by Means of Periodate Oxidation Followed by Cleavage with an Amine," *J. Biol. Chem.* 239:2927-34 (1964);
- Sampson and Uhlenbeck, "Biochemical and physical characterization of an unmodified yeast phenylalanine transfer RNA transcribed *in vitro*," *Proc. Natl. Acad. Sci. USA* 85:1033-37 (1988);

- Hudson, "Methodological Implications of Simultaneous Solid-Phases Peptide Synthesis. 1. Comparison of Different Coupling Procedures," *J. Org. Chem.* 53:617-624 (1988);
- Happ, *et al.*, "New Approach to the Synthesis of 2'(3')-*O*-Aminoacyl Oligoribonucleotides," *J. Org. Chem.* 52:5387-91 (1987);
- Heckler *et al.*, "T4 RNA Ligase Mediated Preparation of Novel "Chemically Misacylated" tRNA ^{Phe}s," *Biochemistry* 23:1468-73 (1984);
- Heckler *et al.*, "Preparation of 2'(3')-O-Acyl-pCpA Derivatives as Substrates for T4 RNA Ligase-Mediated "Chemical Aminoacylation"," *Tetrahedron* 40:87-94 (1984);
- DiCesare, *et al.*, "A High-Sensitivity Electrochemiluminescence-Based Detection System for Automated PCR Product Quantitation," *BioTechniques* 15:152-59 (1993);
- Allen, *et al.*, Gel Electrophoresis and Isoelectric Focusing of Proteins, Walter de Gruyter, New York 1984, pp. 17-62;
- Stephen, "High-Resolution Preparative SDS-Polyacrylamide Gel Electrophoresis: Fluorescent Visualization and Electrophoretic Elution-Concentration of Protein Bands," *Anal. Biochem.* 65:369-79 (1975);
- Pillai, "Photoremovable Protecting Groups in Organic Synthesis," *Synthesis* 1-26 (1980);
- Patchornik, *et al.*, "Photosensitive Protecting Groups," *J. Am. Chem. Soc.* 92:6333-35 (1970);
- *Antibodies: A Laboratory Manual* (E. Harlow and D. Lane, editors, Cold Spring Harbor Laboratory Press), 1988, pp. 53,72-73;
- Powell, *et al.*, "Molecular Diagnosis of Familial Adenomatous Polyposis," *N. Engl. J. Med.* 329:1982-87 (1993);
- Sonar, *et al.*, Biochem. 32:13777-81, 1993[1];
- Widder, *et al.*, "Magnetic Microspheres: A Model System for Site Specific Drug Delivery in *Vivo*," *Proc. Soc. Exp. Biol. & Med.* 58:141-46 (1978); and

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[1] We have been unable to obtain this reference. If the examiner so requests, we can increase our efforts to obtain a copy.

- Oesterhelt *et. al.*, "Bacteriorhodopsin: a biological material for information processing," *Quart. Rev. Biophys.* 4:425-78 (1991).

Applicants have become aware of the following printed publications which may be material to the examination of this application:

- US 5,614,386 to Metzker, *et al.*, reports the use of BODIPY fluorophores for labeling DNA. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- US 5,215,927 to Berenson, *et al.*, describes a method of immunoselection of cells based on avidin and biotinylated antibody. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- US 5,434,272 to Corrie, *et al.*, describes the synthesis of caged fluorophores based on the dyes fluorescein and rhodamine. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- European Pat. No. 0234799A2 to Kurzchalia, *et al.*, describes methods for the detection and isolation of protein utilizing the incorporation of photoaffinity reagents and biotin or other haptens into the lysine residues of nascent peptides. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step and the binding of the nascent protein to a surface.
- U.S. Pat. No. 4,675,285 to Clark, *et al.*, describes a method for identification of clones expressing the desired protein from the cDNA libraries. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Sonar, S., *et al.*, "Cell-Free Synthesis, Functional Refolding and Spectroscopic Charateristics of Bacteriorhodopsin, an Integral Membrane Protein," *Biochemistry* 32:13777-13781 (1993) report on the cell-free synthesis of the protein bacteriorhodopsin. The publication does not disclose the

misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.

- Karolin, J., *et al.*, "Flourescene and Absorption Spectroscopic Properties of Dipyrromethene boron Difluoride (BODIPY) Derivatives in Liquids, lipid Membranes and Proteins," *J. Am. Chem. Soc.* 116:7801-7806 (1994) report on the spectroscopic properties of BODIPY in proteins. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Kurzchalia, T.V., *et al.*, "tRNA-Mediated Labelling of Proteins with Biotin. A Nonradioactive Method for the Detection of Cell-Free Translation Products," *Eur. J. Biochem.* 172:663-668 (1988) report on cell-free translation of proteins made with a modified lysyl-tRNA and biotin label. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step and binding the nascent protein to a surface.
- Baldini, *et al.*, "Mischarging *Escherichia coli* $tRNA^{Phe}$ with L-4'-[3-Trifluoromethyl)-3*H*-diazirin-3-yl]phenylalaine, a Photoactivatable Analogue of Phenylalanine," *Biochemistry* 27:7951-7959 (1988) report a procedure for the misaminoacylation of tRNA with a photoactivatable analog of phenylalanine. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Hall, *et al.*, "Mapping Labeled Sites in *Escherichia coli* Ribosomal RNA: Distribution of Methyl Groups and Identification of a Photoaffinity-Labeled RNA Region Putatively at the Peptidyltransferase Center," *Biochemistry* 24:5702-5711 (1985) report a method utilizing radiolabeled 5-Azido-2-nitrobenzoyl-[H^3]Phe-$tRNA^{Phe}$ to determine structural characteristics of the rRNA in ribosomes. [H^3] was detected by electrophoresis of the rRNA. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Billington, *et al.*, "Synthesis and Photochemistry of Photolabile *N*-Glycine Derivatives and Efforts of One on the Glycine Receptor," *Biochemistry* 31:5500-5507 (1992) report the synthesis of photolabile derivatives of *N*-

glycine. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.

- Mouton, *et al.*, "A Reagent for Covalently Attaching Biotin to Proteins via a Cleavable Connector Arm," *Archives of Biochemistry and Biophysics* 218(1):101-108 (1982) report procedures for the attachment of biotin to proteins via a cleavable connector arm. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Thiele and Fahernholz, "Photocleavable Biotinylated Ligands for Affinity Chromatography," *Analytical Biochemistry* 218:330-337 (1994) report a procedure utilizing biotinylated ligands for affinity chromatography. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Herman, *et al.*, "Affinity Chromatography of DNA Labeled with Chemically Cleavable Biotinylated Nucleotide Analogs," *Analytical Biochemistry* 156:48-55 (1986) report methods for the affinity chromatography of DNA labeled with chemically cleavable biotinylated nucleotide analogs. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Perri, *et al.*, "Tandem Photochemical Synthesis of N-Amino β-Lactams from Pyrazolidin-3-ones," *J. Org. Chem.* 55:6037-6047 (1990) report the photochemical synthesis of N-amino beta-lactams from pyrazolidin-3-ones. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Amit, *et al.*, Photosensitive Protecting Groups of Amino Sugars and Their Use in Glycoside Synthesis. 2-Nitrobenzyloxcarbonylamino and 6-Nitroveratryloxycarbonylamino Derivatives," *J. Org. Chem.* 39(2):192-196 (1974) report the use of 2-nitrobenzyloxycarbonyl and 6-nitroveratryloxycarbonyl as protecting groups for the amino function in amino sugars. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.

- Zehavi, *et al.*, "Light-Sensitive Glycosides. I. 6-Nitroveratryl β-D-Glucopyranoside and 2-Nitrobenzyl β-D-Glucopyranoside," *J. Org. Chem.* 37(14):2281-2285 (1972) report the production and characterization of two light sensitive glucosides, 2-nitrobenzyl beta-D-glucopyranoside and 6-nitroveratryl. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Peyser and Flechtner, "*N*-(α-Hydroxy-2-nitrosobenzyl)-1-naphthamide: A Photochemical Intermediate," *J. Org. Chem.* 25:4645-4646 (1987) report the synthesis of an unstable nitro compound intermediate resulting from the irradiation of N-(2-nitrobenzyl)-1-naphthamide. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Ohtsuka, *et al.*, "Studies on Transfer Ribonucleic Acids and Related Compounds. 20. A New Versatile Ribooligonucleotide Block with 2'-(o-Nitrobenzyl) and 3'-Phosphorodianilidate Groups Suitable for Elongation of Chains in the 3' and 5' Directions," *J. Am. Chem. Soc.* 100(14):4580-4584 (1978) report methods to protect the 2'-hydroxyl group of ribonucleotides during the synthesis of ribonucleotides. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Mendel, *et al.*, "Construction of a Light-Activated Protein by Unnatural Amino Acid Mutagenesis," *J. Am. Chem. Soc.* 113:2758-2760 (1991) report the construction of a tRNA for use in the *in vitro* translation synthesis of a caged T4L lysozyme. The modified lysozyme is inactive until irradiated where upon the enzyme gains full activity. The modified, activated lysozyme is detected by its ability to lyse E. coli by donating a proton to the interglycosidic oxygen of beta(1→4)-linked NAM-NAG residues in the cell wall thereby giving a visual readout. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step and binding the nascent protein to a surface.

- Robertson, *et al.*, "A General and Efficient Route for Chemical Aminoacylation of Transfer RNAs," *J. Am. Chem. Soc.* 113:2722-2729 (1991) report a method for the misaminoacylation of tRNA. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Miknis and Williams, "Total Synthesis of (±)-Aspirochlorine," *J. Am. Chem. Soc.* 115:536-547 (1993) report the synthesis of (±)-aspirochlorine which utilized a 2-nitrobenzyl group as an amide protecting group. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Dawson, *et al.*, "Affinity Isolation of Transcriptionally Active Murine Erythroleukemia Cell DNA Using a Cleavable Biotinylated Nucleotide Analog," *J. Biological Chemistry* 264:12830-12837 (1989) report a method for the affinity isolation of transcriptionally active cellular DNA using a biotinylated nucleotide analog. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Markings and Tsien, "Caged Nitric Oxide, Stable organic Molecules from which Nitric Oxide can be Photoreleased," *J. Biological Chemistry* 269:6282-6285 (1994) report the synthesis and testing of a series of caged nitric oxide compounds. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Thompson, *et al.*, "Photocleavable Nitrobenzyl-Protein Conjugates," *Biochemical and Biophysical Research Communications* 201(3):1213-1219 (1994) report on the synthesis of photocleavable nitrobenzyl-protein conjugates. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Albarella, *et al.*, "Monoadduct forming photochemical reagents for labeling nucleic acids for hybridization," *Nucleic Acids Research* 117(11):4293-4308 (1989) report the synthesis of novel photoreagents for use in the labeling of DNA with biotin. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.

- Robertson, *et al.*, "The use of 5'-phospho-2 deoxyribocytidylylriboadenosine as a facile route to chemical aminoacylation of tRNA," *Nucleic Acids Research* 17(23):9649-9660 (1989) report a method of misaminoacylating tRNA, performing *in vitro* translation with the misaminoacylated tRNA, and detecting the translated protein with incorporation of [^{35}S] Met into the nascent peptide during translation. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step and binding the nascent protein to a surface.
- Lesnikowski and Jaworska, "Studies on Stereospecific Formation of P-Chiral Internucleotide Linkage. Synthesis of (Rp,Rp)- and (Sp,Sp)-Thymidylyl(3',5') Thymidylyl (3',5') Thymidine DI(O,O-Phosphorothioate) using 2-Nitrobenzyl Group as a New S-Protection," *Tetrahedron Letters* 30(29):3821-3824 (1989) report studies on the stereospecific formation of p-chiral internucleotide linkages. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Renil and Pillai, "Synthesis of fully Protected Peptides on a Tetraethyleneglycol Diacrylate (TTEGDA)-Crosslinked Polystyrene support with a Photolytically Detachable 2-Nitrobenzyl Anchoring group," *Tetrahedron Letters* 35(22):3809-3812 (1994) report the synthesis of full peptides on solid support that are released by photolytic cleavage. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Zehavi and Herchman, "Enzymic synthesis of oligosaccharides on a polymer support, light-sensitive, water-soluble substituted poly(vinyl alcohol)," *Carbohydrate Research* 128:160-164 (1984) report an improvement in the synthesis of saccharide derivatives wherein the resulting oligonucleotide is released by irradiation. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Whitney, R.A., "A Photochemical approach to the synthesis of (±)-biotin," *Can. J. Chem.* 59:2650-2653 (1981) reports the synthesis of (±)-biotin utilizing

oxidative rearrangement. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.

- Nishikubo, *et al.*, "Study of Photopolymers. XXXIV. Etherification and Esterification Reactions of Polymers with (*o*, *m*, or *p*)-Bromomethylnitrobenzene Using the DBU Method and the Photochemical Properties of the Resulting Polymers," *J. Polymer Science: Part A: Polymer Chemistry* 28:105-117 (1990) report the successful reaction of poly(4-hydroxystyrene) (PHST) and PMAA with *o*-, *m*- or *p*-bromomethylnitrobenzenes using the DBU method in aprotic polar solvents and studies the photochemical properties of the resulting polymers. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Zehavi, *et al.*, "Enzymic Synthesis of Oligosaccharides on a Polymer Support Light-Sensitive, Substituted Polyacrylamide Beads," *Carbohydrate Research* 124:23-34 (1983) report the enzymatic synthesis of two light-sensitive oligosaccharides on a polymer support. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Ohtsuka, *et al.*, "Studies on Transfer Ribonucleic Acids and Related Compounds; XVIII. A Photolabile 2'-Ether of Guanosine as an Intermediate for Oligonucleotide Synthesis," *Synthesis* 7:453-454 (1977) report the characterization of a photolabile 2'-ether of guanosine as an intermediate for oligonucleotide synthesis. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Yen, *et al.*, "Optically controlled ligand delivery, 1: Synthesis of Water-soulable Copolymers Containing Photocleavable Bonds," *Makromol. Chem.* 190:69-82 (1989) report the synthesis of photocleavable polymers for potential use in immunoassays. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.

- Wilchek and Bayer, "Applications of Avidin-Biotin Technology: Literature Survey," *Methods in Enzymology* 184:14-45 (1990) report the use of avidin-biotin technology for protein identification, analysis and purification. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Houlihan, *et al.*, "Nitrobenzyl Ester Chemistry for Polymer Processes Involving Chemical Amplification," *Maromolecules* 21:2001-2006 (1988) report the synthesis of 2-nitrobenzyl, 2,4-dinitrobenzyl and 2,6-dinitrobenzyl tosylate for use as photochemically labile protective groups. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Chemical Analysis, Hemmila, "Application of Fluorescence in Immunoassays," p139-158, reports the physical characteristics and methods of quantification of various organometallic fluorochromes. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Kozak, "Point Mutations Define a Sequence Flanking the AUG Initiator Codon that Modulates Translation by Eukaryotic Ribosomes," *Cell* 44:283-292 (1986) reports a sequence flanking the AUG initiator codon that modulates eukaryotic ribosomes. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Odom, *et al.*, Methods in Molecular Biology "In Vitro Engineering Using Acyl-Derivatized tRNAs," edited by:R. Matin Humana Press Inc., Totowa, NJ Chapter 7, pp.93-103, report the synthesis of CPM-SAc-[^{35}S]Met-tRNA$_f$ by successive reactions of [^{35}S]Met-tRNA with DTDG monosuccinimidyl ester, DTT and CPM. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Varshney, *et al.*, "Initiation of protein synthesis from a termination codon," *PNAS* 87:1586-1590 (1990) report the use of a misaminoacylation of a tRNA to demonstrate that translation can begin with a termination codon. The publication does not disclose the misaminoacylation of tRNA with a non-

radioactive marker followed by a translation step and binding the nascent protein to a surface.

- Varshney, *et al.*, "Direct Analysis of Aminoacylation Levels of tRNAs in Vivo," *J. Biological Chemistry* 266(36):24712-24718 (1991) report methods of detecting aminoacylation levels of tRNAs *in vivo* using mutated tRNAs and gel electrophoresis. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step and bonding the nascent protein to a surface.
- Krafft, *et al.*, "Photoactivable Fluorophores. 3. Synthesis and Photoactivation of Fluorogenic Difunctionalized Fluoresceins," *J. Am. Chem. Soc.* 110:301-303 (1988) report the synthesis of a photoactivatable fluorophore designed for tracer studies of molecular transport and diffusion in biological systems. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Kalbag and Roeske, "A Photolabile Protecting Group for Histidine," *J. Am. Chem. Soc.* 97:440-441 (1975) reports the synthesis wherein the *o*-nitrobenzyl group of imidazole was introduced into the side chain of histidine and subsequently removal by irradiation. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Crowley, *et al.*, "The signal sequence moves through a ribosomal tunnel into a noncytoplasmic aqueous environment at the ER membrane early in translocation," *Cell* 73:1101-1115 (1993). This reference reports the logistics of nascent peptide production by utilizing [^{14}C]Lys-tRNA analogs to incorporate fluorescent probes into the signal sequence to examine the environment of a nascent peptide chain as it moved through the ribosome and into the ER membrane. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step and binding the nascent protein to a surface.
- Hardesty, *et al.*, "Extension and Folding of Nascent Peptides on Ribosomes." The Translational Apparatus, Nierhaus *et al.* ed: New York and London;

Plenum Press. p.347-358 (1993) report peptide folding experiments where amino-tRNAs were modified after aminoacylation. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step and binding the nascent protein to a surface.

- Johnson, *et al.*, "Protein Synthesis and Secretion as seen by the Nascent Protein Chain," The Translational Apparatus, Nierhaus *et al.* ed: New York and London; Plenum Press. p. 359-370 (1993) report peptide synthesis experiments where Lys-tRNA was modified after aminoacylation. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step and binding the nascent protein to a surface.
- Czworkowski, *et al.*, "Fluorescence Study of the Topology of Messenger RNA Bound to the 30S Ribosomal Subunit of *Escherichia coli*," *Biochemistry* 30:4821-4830 (1991), report the interaction of fluorescently labeled RNAs (25-36 nucleotides in length) with the fluorescently labeled 30S subunit of Escherichia coli was studied by using fluorescence spectroscopic techniques. By using the distances calculated from energy transfer a topological map of this region of mRNA on the 30S subunit was constructed. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Hardesty, *et al.*, "Ribosome function determined by fluorescence," *Biochimie* 74:391-401 (1992), report on the fluorescence spectroscopy and fluorescent resonance energy transfer and their application to the studies on the structure, movement and conformation of tRNA, the nascent peptide, and mRNA in a ribosome during the reaction steps of peptide elongation. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step and and binding the nascent protein to a surface.
- Kudlicki, *et al.*, "Chaperone-dependent Folding and Activation of Ribosome-bound Nascent Rhodanese," *J. Mol. Biol.* 244:319-331 (1994), report on the synthesis of coumarin labeled rhodanese by coupled transcription/translation in a cell-free Escherichia coli system. The influence of chaperones on the release of nascent rhodanese from ribosome was studied by fluorescence spectroscopy.

The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.

- Picking, *et al.*, "The use of synthetic tRNA as probes for examining nascent peptides on *Escherichia coli* ribosomes," *Biochimie* 73:1101-1107 (1991), the cell free synthesis of N-acetyl or N-acyl coumarin labeled polycysteine and polyserine was carried out on Escherichia coli ribosomes using N-acyl coumarin derivatives of either Ser-tRNA or Phe-tRNA. The properties of the resulting nascent peptides were studied by fluorescence spectroscopy and compared to those of nascent polyphenylalanine chains synthesized under similar conditions. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step and and binding the nascent protein to a surface.
- Picking, *et al.*, "Evidence for RNA in the Peptidyl Transferase Center of *Escherichia coli* Ribosomes as Indicated by Fluorescence," *Biochemistry* 31:12565-12570 (1992). The interaction of coumarin labeled (tRNA(phe)) [either the amino acid or the 5' end] with ribosomes was studied using fluorescence spectroscopy. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step and and binding the nascent protein to a surface.
- Picking, *et al.*, "The Conformation of Nascent Polylysine and Polyphenylalanine Peptides on Ribosomes," *J. Biol. Chem.* 266:1534-1542 (1991), report the behavior of fluorescently labeled polylysine and polyphenylalanine during their *in vitro* synthesis on *E. coli* ribosomes. The position and conformation of the nascent peptide were monitored by fluorescence techniques. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step and binding the nascent protein to a surface.
- Picking, *et al.*, "Fluorescence Characterization of the Environment Encountered by Nascent Polyalanine and Polyserine as They Exit *Escherichia coli* Ribosomes during Translation," *Biochemistry* 31:2368-2375 (1992) report that a coumarin probe placed at the alpha-amino group of a synthetic elongator

alanyl-tRNA or a synthetic initiator alanyl-tRNA or at the epsilon-amino group of natural lysyl-tRNA, and each was used to nonenzymatically initiate peptide synthesis. The interaction of nascent polypeptides with the environments was studied using fluorescence techniques. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step and binding the nascent protein to a surface.

- Picking, *et al.*, "A synthetic alanyl-initiator tRNA with initiator tRNA properties as determined by fluorescence measurements: Comparison to a synthetic alanyl-elongator tRNA," *Nucleic Acids Research* 19:5749-5754 (1991) report that a derivative of coumarin was covalently attached to the alpha amino group of alanine of the two synthetic Ala-tRNA species. The fluorescence spectra, quantum yield and anisotropy for the two Ala-tRNA derivatives were studied after they were bound to 70S ribosomes. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step and binding the nascent protein to a surface.
- Ma, *et al.*, "*In Vitro* Protein Engineering Using Synthetic $tRNA^{Ala}$ with Different Anticodons," *Biochemistry* 32:7939-7945 (1993), report that synthetic tRNA for *in vitro* protein engineering was tested in a coupled transcription/translation system prepared from *Escherichia coli.* Markers were not attached to the alpha-amino acid. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step and binding the nascent protein to a surface.
- Odom, *et al.*, "Movement of tRNA but Not the Nascent Peptide during Peptide Bond Formation on Ribosomes," *Biochemistry* 29:10734-10744 (1990), report the interaction of fluorescently labeled (Phe) tRNA (labeled at the 5'-end) with the ribosome as well as with the nascent polypeptide, was investigated using nonradiative energy transfer. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step and binding the nascent protein to a surface.
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- Bain, *et al.*, "Site-Specific Incorporation of Nonnatural Residues into Peptides: Effect of Residue Structure on Suppression and Translation Efficiencies" *Tetrahedron* 47:2389-2400 (1991), report on a method for the incorporation of misaminoacylation of tRNA with an amino acid comprising a radioactive tag. Incorporation of the amino acid into a peptide is determined by precipitation and detection of radioativity by scintillation counting. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
- Johnson, *et al.*, "N^{ε}-Acetyllysine Transfer Ribonucleic Acid: A Biologically Active Analogue of Aminoacyl Tranfer Ribonucleic Acids" *J Am Chem Soc* 15:569-575 (1976), report a method for the preparation an analogue of Lys-tRNA (ε-Ac-Lys-tRNA) for the transfer of the modified amino acid into a nascent peptide chain. Incorporated amino acids were detected by scintillation counter. The publication does not disclose the misaminoacylation of tRNA with a non-radioactive marker followed by a translation step.
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This Information Disclosure Statement under 37 C.F.R. §§ 1.56 and 1.97 is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one or more of these citations constitutes prior art.

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